# WEST Search History

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DATE: Friday, January 28, 2005

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
| | *DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ* | | |
| ☐ | L8 | L5 and CCR5 | 26 |
| ☐ | L7 | L6 and (CC-CKR5) | 3 |
| ☐ | L6 | L5 and HIV | 235 |
| ☐ | L5 | L4 | 722 |
| | *DB=PGPB,USPT,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ* | | |
| ☐ | L4 | L3 and R5 | 2234 |
| ☐ | L3 | antibody | 204532 |
| ☐ | L2 | L1 and CCR5 | 3 |
| ☐ | L1 | Wu L.in. | 789 |

END OF SEARCH HISTORY

=> file caplus biosis
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'CAPLUS' ENTERED AT 06:43:09 ON 28 JAN 2005
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FILE 'BIOSIS' ENTERED AT 06:43:09 ON 28 JAN 2005


=> antibody
L1 989892 ANTIBODY

=> CCR5
L2 6393 CCR5

=> "CC CKR5"
L3 35 "CC CKR5"

=> L1 and L2
L4 1147 L1 AND L2

=> L1 (s) L2
L5 536 L1 (S) L2

=> L1 and L3
L6 7 L1 AND L3

=> D L6 IBIB ABS 1-6
=> L5 and 2D7
L7 33 L5 AND 2D7

=> L5 and inhibition
L8 73 L5 AND INHIBITION

=> L8 and HIV
L9 58 L8 AND HIV

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:772659 CAPLUS
DOCUMENT NUMBER: 128:33766
TITLE: Methods of identifying G-coupled receptors associated with macrophage-trophic HIV, and diagnostic and therapeutic uses thereof
INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried; Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9744055 | A1 | 19971127 | WO 1997-US8926 | 19970520 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5939320 | A | 19990817 | US 1996-666020 | 19960619 |
| AU 9731434 | A1 | 19971209 | AU 1997-31434 | 19970520 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1996-17157P | P | 19960520 |
| US 1996-650412 | A | 19960520 |
| US 1996-666020 | A | 19960619 |
| WO 1997-US8926 | W | 19970520 |

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is **CC-CKR5**, a receptor for the β-chemokines RANTES, MIP-1α, and MIP-1β. The cofactor is useful for screening of drugs capable of modulating the production of a translocation promoting agent and capable of treating AIDS.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:229024 CAPLUS
DOCUMENT NUMBER: 128:279581
TITLE: Cloning, sequence, and expression of a mouse genomic clone for the **CC-CKR5** receptor and construction of knockout mutations
INVENTOR(S): Bergsma, Derk J.; Brawner, Mary E.; Shabon, Usman
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 834564 | A2 | 19980408 | EP 1997-307823 | 19971003 |
| EP 834564 | A3 | 19980513 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6388055 | B1 | 20020514 | US 1996-724984 | 19961003 |
| JP 10179180 | A2 | 19980707 | JP 1997-307784 | 19971003 |
| PRIORITY APPLN. INFO.: | | | US 1996-724984 A | 19961003 |

AB Mouse chemokine receptor **CC-CKR5** polypeptides and DNA (RNA) encoding such mouse **CC-CKR5** and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such mouse **CC-CKR5** in the development of gene knockout mice for use as a model for human immunodeficiency virus.. Expression vectors carrying the **CC-CKR5** gene are constructed and expressed in human embryonic kidney 293 cells. **Antibodies** to **CC-CKR5** are also claimed.

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:499783 CAPLUS
DOCUMENT NUMBER: 135:103329
TITLE: Methods of identifying G protein-coupled receptors associated with the uptake of macrophage-trophic HIV, and their use in diagnosis and treatment of AIDS
INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried; Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S): The Aaron Diamond Aids Research Center, USA; New York University
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 858,660, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 6258527 | B1 | 20010710 | US 1997-861105 | | 19970521 |
| US 2003096221 | A1 | 20030522 | US 2000-734221 | | 20001211 |
| PRIORITY APPLN. INFO.: | | | US 1996-17157P | P | 19960520 |
| | | | US 1996-20043P | P | 19960619 |
| | | | US 1997-858660 | B2 | 19970519 |
| | | | US 1997-861105 | A1 | 19970521 |

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is **CC-CKR5**, a receptor for the β-chemokines RANTES, MIP-1α, and MIP-1β. The uptake of the virus may be blocked by ligands for the receptor or by preventing the receptor gene expression and in control of the synergism between infection by other viruses and the spread of HIV into other cell types. Expts. with viruses pseudotyped with different env glycoproteins showed that uptake was dependent upon the presence of chemokine receptors with different serotypes of the virus showing different receptor requirements. Methods of using chemokine receptor-deficient host cells as expression hosts to identify receptor requirements of clin. isolates of HIV-1 are described.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:185460 CAPLUS
DOCUMENT NUMBER: 132:333214
TITLE: **Inhibition** of M-tropic **HIV**-1 infection by the fd phage-gene 3 protein with MIP-1α-binding activity
AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering, Kagoshima University, Kagoshima, 890-0063, Japan
SOURCE: Molecular Immunology (2000), Volume Date 1999, 36(18), 1249-1254
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of **HIV**-1. The anti-**CCR5** monoclonal **antibody** (mAb) **2D7** inhibits the binding and chemotaxis of the three natural β-chemokine ligands of **CCR5**, macrophage inflammatory protein (MIP)-1α, MIP-1β, and RANTES, to **CCR5**+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic **HIV**-1 strains in vitro. In this study, the authors attempted to determine the peptide motif recognized with the **2D7** mAb. The authors isolated phage clones by panning a phage display library using **2D7** and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on **HIV**-1 infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatog. (FPLC). The authors show here that (1) M23-g3p was specifically recognized with anti-CCR5 mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic **HIV**-1 strains; (3) M23-g3p bound to MIP-1α, MIP-1β, and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by β-chemokines, MIP-1α, MIP-1β, and RANTES as well as the **HIV**-1 infection.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:263464 CAPLUS
DOCUMENT NUMBER: 131:57557
TITLE: Differential **inhibition** of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal **antibodies** to **CCR5**
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (**HIV**-1) strains. The authors have isolated 6 new anti-**CCR5** murine

monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) **HIV**-1 entry, (2) **HIV**-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit **HIV**-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV**-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and **2D7**, the most potent inhibitors of **HIV**-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV**-1 entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-IgG2, which inhibits **HIV**-1 attachment. The data support a model wherein **HIV**-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:683672 CAPLUS
DOCUMENT NUMBER: 127:357954
TITLE: Interaction of chemokine receptor CCR5 with its ligands: multiple domains for **HIV**-1 gp120 binding and a single domain for chemokine binding
AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard; Humblias, Jason; Samson, Michel; Parmentier, Marc; Moore, John P.; Mackay, Charles R.
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Experimental Medicine (1997), 186(8), 1373-1381
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic strains of **HIV**-1. To understand the mol. basis of the binding of chemokines and **HIV**-1 to CCR5, we developed a number of mAbs that inhibit the various interactions of CCR5, and mapped the binding sites of these mAbs using a panel of CCR5/CCR2b chimeras. One mAb termed **2D7** completely blocked the binding and chemotaxis of the three natural chemokine ligands of CCR5, RANTES (regulated on activation normal T cell expressed and secreted), macrophage inflammatory protein (MIP)-1α, and MIP-1β, to CCR5 transfectants. This mAb was a genuine antagonist of CCR5, since it failed to stimulate an increase in intracellular calcium concentration in the CCR5 transfectants, but blocked calcium responses elicited by RANTES, MIP-1α, or MIP-1β. This mAb inhibited most of the RANTES and MIP-1α chemotactic responses of activated T cells, but not of monocytes, suggesting differential usage of chemokine receptors by these two cell types. The **2D7** binding site mapped to the second extracellular loop of CCR5, whereas a group of mAbs that failed to block chemokine binding all mapped to the NH2-terminal region of CCR5. Efficient **inhibition** of an M-tropic **HIV**-1-derived envelope glycoprotein gp120 binding to CCR5 could be achieved with mAbs recognizing either the second extracellular loop or the

NH2-terminal region, although the former showed superior **inhibition**. Addnl., **2D7** efficiently blocked the infectivity of several M-tropic and dual-tropic **HIV**-1 strains in vitro. These results suggest a complicated pattern of **HIV**-1 gp120 binding to different regions of CCR5, but a relatively simple pattern for chemokine binding. We conclude that the second extracellular loop of CCR5 is an ideal target site for the development of inhibitors of either chemokine or **HIV**-1 binding to CCR5.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:177648 BIOSIS
DOCUMENT NUMBER: PREV200000177648
TITLE: **Inhibition** of M-tropic **HIV**-1 infection by the fd phage-gene 3 protein with MIP-1alpha-binding activity.
AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa [Reprint author]
CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering, Kagoshima University, 1-21-40 Korimoto, Kagoshima, 890-0063, Japan
SOURCE: Molecular Immunology, (Dec., 1999) Vol. 36, No. 18, pp. 1249-1254. print.
CODEN: MOIMD5. ISSN: 0161-5890.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 May 2000
Last Updated on STN: 4 Jan 2002

AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of **HIV**-1. The anti-**CCR5** monoclonal **antibody** (mAb) **2D7** inhibits the binding and chemotaxis of the three natural beta-chemokine ligands of **CCR5**, macrophage inflammatory protein (MIP)-1alpha, MIP-1beta, and RANTES, to **CCR5**+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic **HIV**-1 strains in vitro. In this study, we attempted to determine the peptide motif recognized with the **2D7** mAb. We isolated phage clones by panning a phage display library using **2D7** and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on **HIV**-1 infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatography (FPLC). We show here that (1) M23-g3p was specifically recognized with anti-CCR5 mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic **HIV**-1 strains; (3) M23-g3p bound to MIP-1alpha, MIP-1beta, and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by beta-chemokines, MIP-1alpha, MIP-1beta, and RANTES as well as the **HIV**-1 infection.

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1999:238925 BIOSIS
DOCUMENT NUMBER: PREV199900238925
TITLE: Differential **inhibition** of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal **antibodies** to **CCR5**
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana [Reprint author]

CORPORATE SOURCE: Aaron Diamond AIDS Research Center, 455 1st Ave., 7th Floor, New York, NY, 10016, USA
SOURCE: Journal of Virology, (May, 1999) Vol. 73, No. 5, pp. 4145-4155. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (**HIV**-1) strains. We have isolated six new anti-**CCR5** murine monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (i) **HIV**-1 entry, (ii) **HIV**-1 envelope glycoprotein-mediated membrane fusion, (iii) gp120 binding to CCR5, and (iv) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit **HIV**-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9 to PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV**-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and **2D7**, the most potent inhibitors of **HIV**-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV**-1 entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-immunoglobulin G2, which inhibits **HIV**-1 attachment. The data support a model wherein **HIV**-1 entry occurs in three stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. The antibodies described will be useful for further dissecting these events.

L11 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:683672 CAPLUS
DOCUMENT NUMBER: 127:357954
TITLE: Interaction of chemokine receptor CCR5 with its ligands: multiple domains for HIV-1 gp120 binding and a single domain for chemokine binding
AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard; Humblias, Jason; Samson, Michel; Parmentier, Marc; Moore, John P.; Mackay, Charles R.
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Experimental Medicine (1997), 186(8), 1373-1381
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Interaction of chemokine receptor CCR5 with its ligands: multiple domains for HIV-1 gp120 binding and a single domain for chemokine binding
AU Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard; Humblias, Jason; Samson, Michel; Parmentier, Marc; Moore, John P.; Mackay, Charles R.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:353334 CAPLUS
DOCUMENT NUMBER: 131:169077
TITLE: Peptide-motif analysis of phage clones selected by anti-**CCR5** monoclonal **antibody** ( **2D7**)
AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering, Kagoshima University, Kagoshima, 890-0065, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 489-492
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
TI Peptide-motif analysis of phage clones selected by anti-**CCR5** monoclonal **antibody** (**2D7**)
AU Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 127:357954
TITLE: Interaction of chemokine receptor CCR5 with its ligands: multiple domains for **HIV**-1 gp120 binding and a single domain for chemokine binding
AUTHOR(S): Wu, Lijun; LaRosa, Greg; Kassam, Nasim; Gordon, Cynthia J.; Heath, Heidi; Ruffin, Nancy; Chen, Howard; Humblias, Jason; Samson, Michel; Parmentier, Marc; Moore, John P.; Mackay, Charles R.
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Experimental Medicine (1997), 186(8), 1373-1381
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic strains of **HIV**-1. To understand the mol. basis of the binding of chemokines and **HIV**-1 to CCR5, we developed a number of mAbs that inhibit the various interactions of CCR5, and mapped the binding sites of these mAbs using a panel of CCR5/CCR2b chimeras. One mAb termed **2D7** completely blocked the binding and chemotaxis of the three natural chemokine ligands of CCR5, RANTES (regulated on activation normal T cell expressed and secreted), macrophage inflammatory protein (MIP)-1α, and MIP-1β, to CCR5 transfectants. This mAb was a genuine antagonist of CCR5, since it failed to stimulate an increase in intracellular calcium concentration in the CCR5 transfectants, but blocked calcium responses elicited by RANTES, MIP-1α, or MIP-1β. This mAb inhibited most of the RANTES and MIP-1α chemotactic responses of activated T cells, but not of monocytes, suggesting differential usage of chemokine receptors by these two cell types. The **2D7** binding site mapped to the second extracellular loop of CCR5, whereas a group of mAbs that failed to block chemokine binding all mapped to the NH2-terminal region of CCR5. Efficient **inhibition** of an M-tropic **HIV** -1-derived envelope glycoprotein gp120 binding to CCR5 could be achieved with mAbs recognizing either the second extracellular loop or the NH2-terminal region, although the former showed superior **inhibition**. Addnl., **2D7** efficiently blocked the infectivity of several M-tropic and dual-tropic **HIV**-1 strains in vitro. These results suggest a complicated pattern of **HIV**-1 gp120 binding to different regions of CCR5, but a relatively simple pattern for chemokine binding. We conclude that the second extracellular loop of CCR5 is an ideal target site for the development of inhibitors of either chemokine or **HIV**-1 binding to CCR5.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:263464 CAPLUS
DOCUMENT NUMBER: 131:57557
TITLE: Differential **inhibition** of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal **antibodies** to **CCR5**
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (**HIV**-1) strains. The authors have isolated 6 new anti-**CCR5** murine monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) **HIV**-1 entry, (2) **HIV**-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit **HIV**-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited **HIV**-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and **2D7**, the most potent inhibitors of **HIV**-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting **HIV**-1 entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-IgG2, which inhibits **HIV**-1 attachment. The data support a model wherein **HIV**-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:459509 CAPLUS
DOCUMENT NUMBER: 127:173725
TITLE: Development of resistance of human immunodeficiency virus type 1 to dextran sulfate associated with the emergence of specific mutations in the envelope gp 120 glycoprotein
AUTHOR(S): Este, Jose A.; Schols, Dominique; De Vreese, Karen; Van Laethem, Kristel; Vandamme, Anne-Mieke; Desmyter, Jan; De Clercq, Erik
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Molecular Pharmacology (1997), 52(1), 98-104
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyanionic compds. are known to inhibit the binding of human immunodeficiency virus (HIV) to CD4+ cells and the subsequent fusion step between the virus and cells. An HIV-1 strain resistant to dextran sulfate (DS) was selected by cultivation of HIV-1 (NL4-3)-infected MT-4 cells in the presence of DS Mr 5000. DS did not inhibit the binding of DS-resistant virus to MT-4 cells or syncytium formation between MOLT cells and HUT-78 cells persistently infected with the DS-resistant virus. In addition, a monoclonal **antibody** with specificity for the V3 loop of envelope gp120 glycoprotein did not recognize the DS-resistant HIV-1 gp120 V3 loop. The following mutations were found in the gp120 mol. of the DS-resistant HIV-1 strain but not in the wild-type strain: S114N in the V1 loop region; S134N in the V2 loop region; K269E, Q278H, and N293D in the V3 loop region; N323S in the C3 region; a deletion of 5 amino acids (Phe-Asn-Ser-Thr-Trp) at positions 364-368 in the V4 loop; and R3871 in the CD4 binding domain. These results suggest that (i) DS interacts with specific amino acid residues in the gp 120 mol., (ii) the virus is able to overcome the inhibitory effect of DS on viral infectivity, (iii) cross-resistance developed against those polyanionic compds. that are structurally related to DS, and (iv) the mol. determinants of HIV cell tropism, syncytium-inducing ability, coreceptor (fusin/**CC-CKR5**) utilization, and polyanion resistance seem to be located in the env genome of HIV and specifically in the V3 loop domain.

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:433148 CAPLUS
DOCUMENT NUMBER: 125:112550
TITLE: Cell type-specific fusion cofactors determine human immunodeficiency virus type 1 tropism for T-cell lines versus primary macrophages
AUTHOR(S): Alkhatib, Ghalib; Broder, Christopher C.; Berger, Edward A.
CORPORATE SOURCE: Lab. Viral Dis., Natl. Inst. Allergy and Infectious Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1996), 70(8), 5487-5494
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Work in this laboratory previously demonstrated that the tropism of different human immunodeficiency type 1 isolates for infection of human CD4+ continuous cell lines (e.g., T-cell lines and HeLa-CD4 transformants) vs. primary macrophages is associated with parallel intrinsic fusogenic specificities of the corresponding envelope glycoproteins (Envs). For T-cell line-tropic isolates, it is well established that the target cell must also contain a human-specific fusion cofactor(s) whose identity is unknown. In this study, we tested the hypothesis that the Env fusion specificities underlying T-cell line vs. macrophage tropism are determine

distinct cell type-specific fusion cofactors. We applied a recombinant vaccinia virus-based reporter gene assay for Env-CD4-mediated cell fusion; the LAV and Ba-L Envs served as prototypes for T-cell line-tropic and macrophage-tropic isolates, resp. We examined CD4+ promyelocytic and monocytic cell lines that are infectible by T-cell line-tropic isolates and become susceptible to macrophage-tropic strains only after treatment with differentiating agents. We observed parallel changes in fusion specificity: untreated cells supported fusion by the LAV but not the Ba-L Env, whereas cells treated with differentiating agents acquired fusion competence for Ba-L. These results suggest that in untreated cells, the block to infection by macrophage-tropic isolates is at the level of membrane fusion; furthermore, the differential regulation of fusion permissiveness for the two classes of Envs is consistent with the existence of distinct fusion cofactors. To test this notion directly, we conducted expts. with transient cell hybrids formed between CD4-expressing nonhuman cells (murine NIH 3T3) and different human cell types. Hybrids formed with HeLa cells supported fusion by the LAV Env but not by the Ba-L Env, whereas hybrids formed with primary macrophages showed the opposite specificity; hybrids formed between HeLa cells and macrophages supported fusion by both Envs. These results suggest the existence of cell type-specific fusion cofactors selective for each type of Env, rather than fusion inhibitors for discordant Env-cell combinations. Finally, analyses based on recombinant protein expression and **antibody** blocking did not support the proposals by others that the CD44 or CD26 antigens are involved directly in the entry of macrophage-tropic isolates.

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